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Early View

Original article

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Paediatric cohort studies on lower respiratory diseases and their reporting quality: systematic review of the year 2018

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Take home message: We need a joined effort of editors, reviewers and authors to improve the reporting quality of paediatric cohort studies for respiratory problems.

Conflict of interest: None

Authors contributions: Claudia E Kuehni, Myrofora Goutaki, Cristina Ardura-Garcia, Eva Pedersen, and Rebeca Mozun conceptualised and designed the study. Cristina Ardura-Garcia, Rebeca Mozun, Eva SL Pedersen, Maria Otth, and Maria Christina Mallet performed the screening and data extraction. Cristina Ardura-Garcia analysed the data and drafted the manuscript. All authors critically revised the manuscript and approved the final manuscript as submitted.

Key words: systematic review, paediatric, cohort studies, respiratory symptoms

Abstract

The paediatric respiratory research community uses cohort studies extensively. However, the landscape of these studies and their quality of reporting has not been assessed.

We performed a systematic review of publications on cohort studies reporting on paediatric lower respiratory problems published in 2018. We searched Medline and EMBASE and extracted data on the studies' and journals' characteristics. We assessed the number of items of the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist that a random sample (100 papers) reported. We analysed factors associated with the STROBE score and with the most poorly reported items, using Poisson and logistic regression

Of the 21 319 records identified, 369 full-text articles met our inclusion criteria. Most papers studied asthma aetiology through birth cohorts and were based in Europe or North America. The reporting quality was insufficient: 15% reported the 22 STROBE items; median score: 18 (IQR: 16-21). The most poorly reported items were: sources of bias, sample size, statistical methods, descriptive results and generalisability. None of the studies' or journals' factors were associated with the STROBE score.

We need a joined effort of editors, reviewers and authors to improve the reporting quality of paediatric cohort studies on respiratory problems.

Introduction

Cohort studies are extensively used in paediatric respiratory research to investigate risk factors, incidence and natural history of disease. The strengths of the longitudinal design include establishing temporality and reducing information bias. However, the study design has limitations, like high costs, selection bias, attrition bias, and residual confounding. There are solutions to overcome or mitigate these disadvantages like retrospective cohort design, nested case-control studies or linkage to nationwide available datasets. The use of these strategies, the type of questions investigated and the quality of reporting of cohort studies has not been assessed in paediatric respiratory research.

Adequate reporting is key for reproducibility of research and translation of results into clinical practice. STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) is an international, multidisciplinary and collaborative initiative started in 2004 to enhance the reporting quality and dissemination of observational studies [1]. The STROBE statement is being increasingly endorsed by journals, but mandatory submission of its checklist is not yet common practice for observational studies as it is for randomized controlled trials. Studies assessing the fulfilment of the STROBE criteria suggest that reporting quality is generally poor and that some items are frequently underreported [2-4]. Certain factors have been associated with reporting quality, such as journal's impact factor and STROBE endorsement policy, the authors' affiliation, and publication type (peer reviewed or not) [3,5-7]. Identifying which STROBE items are commonly misreported in paediatric respiratory cohort papers and which modifiable factors are associated with poor reporting may raise awareness and help improve the quality of publications in this area. We therefore conducted a systematic review of papers published in 2018 to present the landscape of cohort studies addressing paediatric lower respiratory problems, to describe the reporting quality of these papers according to STROBE guidelines and to examine characteristics associated with reporting quality.

Methods

The predefined review protocol that we followed for this systematic review has been registered in the Open Science Framework (OSF) repository (Registration DOI 10.17605/OSF.IO/F8X3B). We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, research checklist online) [8] to report our findings.

Eligibility criteria

We searched for papers reporting on lower respiratory problems from paediatric cohort studies worldwide, published in 2018 in peer-reviewed journals. For this we used all the following specific inclusion criteria: (1) cohort study design (exposure measured before outcome, with at least two time points with prospective data collection), including nested case-control studies; (2) children under 18 years of age at study baseline, or with separate results reported for children, or for rare diseases, if more than 50% of the study population were children; (3) lower respiratory problems and evaluations of lower respiratory health as outcomes (including respiratory symptoms, test results such as lung function, diagnosis and prognosis) or lower respiratory problems and evaluations of lower respiratory health as exposures (including respiratory symptoms, test results such as lung function, diagnosis, management and prognosis).

We excluded studies with any of the following criteria: (1) reports not in English, (2) published before 1st January 2018 or after 31st December 2018, (3) non-original papers (conference abstracts, editorials and reviews), (4) follow-up time <3 months (to exclude papers on short-term outcomes of hospitalised patients), and (5) studies with <50 participants to exclude small case series (for rare diseases where smaller sample sizes are expected we excluded if there were <20 participants). If exact sample size was not stated but we could assure that it was greater than our selected limits for paper exclusion, the manuscript was included in the study.

Information sources and search strategy

We searched Medline and EMBASE from 1st January 2018 to 31st December 2018, on April 17th 2019. We used a reference management software (EndNote X8, Thomson Reuters) to import the records and remove duplicates. We provide the full search strategy in the online supplementary information.

Study selection

One reviewer screened titles and abstracts to assess eligibility according to the described criteria. In a second step, a single reviewer screened full-text papers of selected studies and recorded the reasons for exclusion in an Excel form.

Data extraction

We extracted data from the selected papers using a standardised pre-piloted data collection Excel form. We extracted information on the characteristics of the manuscript (author, journal, location and year of publication) and the study (cohort name and size, study design, type of research question, main diseases of interest, source of exposure and outcome data, use of longitudinal analysis, follow-up time and age at baseline). We did not include a risk of bias assessment, as the results were not extracted and evaluated.

Definitions

Journals were classified into thematic categories according to the InCites Journal Citation Report classification. If a journal appeared in two different categories, it was classified as the first in which it appeared in this order: respiratory, allergy, infectious diseases, public health/ epidemiology/ environment, paediatrics, general medicine and any other category (Supplementary Table 1). The diagnoses studied were grouped into: asthma or wheeze, respiratory infectious diseases, rare diseases (defined as occurring in fewer than 1 in 2000

people, and including bronchopulmonary dysplasia, diaphragmatic hernia, cystic fibrosis and primary ciliary dyskinesia), lung function in healthy children and other problems (including cough, respiratory distress syndrome, pneumothorax and unspecific respiratory symptoms).

Assessment of reporting quality

We selected a random sample of 100 (27%) of the included papers and assessed how close the manuscript followed the STROBE recommendations for the reporting of cohort studies. We used a standardised data collection Excel form and recorded the adherence to each of the 22 items present in the STROBE checklist for the reporting of cohort studies. The STROBE statement recommends the reporting of all the elements in their checklist. For this reason, we considered insufficient reporting if not all the elements (22) were reported. We did not evaluate the items that are only 'suggested', such as the inclusion of a flow diagram. We defined an item as not reported if it was not present or insufficiently reported. For example, for item 7, if they defined the outcome and main exposure, but not other variables (e.g. confounders and important effect modifiers). To examine characteristics associated with reporting quality, we also extracted information of variables that have been previously associated with reporting: journal's impact factor, percentage ranking, category, reporting recommendations and if it belonged to a scientific society; and the study's location, research question and main diagnosis of interest. We used data from the InCites Journal Citation Report to record the impact factor and ranking of the journal where the manuscript was published, and from the journals' webpages to collect information on whether the journal belonged to a scientific society and on the reporting recommendations (classified into no recommendation (none), recommending to follow any reporting guideline, recommending to follow STROBE reporting guidelines and mandatory attachment of the STROBE checklist at the time of manuscript submission).

Synthesis of results and analysis

We summarised the results (absolute numbers and proportions) of the study characteristics, the journals where they were published and the reporting quality according to the STROBE statement using tables and graphs. We used Poisson regression to study univariable associations between the study's characteristics and the number of items from the STROBE checklist that were reported in the manuscript. We reported the rate ratio with 95% confidence interval, and the p value of the likelihood ratio test. We then applied logistic regression to study univariable associations between the study's characteristics and the reporting of the 4 items from the STROBE checklist that were most poorly reported: item 9 (bias), item 12 (statistics), item 14 (descriptive results) and item 21 (generalisability). We reported the odds ratio with 95% confidence interval for each item separately. For both regression analyses, we included the following factors based on previous findings and plausibility of association with reporting quality: journal's impact factor, ranking, category, reporting recommendations and if it belonged to a scientific society; and the study's location, research question and main diagnosis of interest.

Results

Of the 15 846 records identified through database searching, 890 were selected based on title and abstract and 369 full-text articles were finally included in the systematic review (Figure 1). Of the 521 full-text articles excluded, 77 were not a cohort study and 24 did not include a longitudinal analysis (e.g. used cross-sectional data from a cohort study).

Most studies were located in Europe (161, 44%) or North America (108, 29%), with few from other locations, especially Africa (17, 5%) and South America (12, 3%) (Figure 2). The median sample size was of 746 children (IQR 187-4535). Forty one percent of the studies had a birth or pregnancy cohort design, followed by prospective clinical cohorts (109, 30%) and non-birth

population-based cohorts (56, 15%). Median follow-up time was 5 years (IQR: 1-10 years). A quarter (85, 23%) used linkage with routine datasets and there were very few nested case-control studies (7, 2%). The most frequent sources of exposure data were questionnaires/ interviews (128, 35%) or direct examination/ diagnostic tests (134, 36%), while outcomes were normally obtained from questionnaires/ interviews (157, 43%).

The main diagnosis of interest in the included studies was asthma or wheeze (214, 58%) and the main research questions related to aetiology (194, 53%) followed by natural history or prognosis (116, 31%). The research questions varied by diagnosis of interest (Figure 3a). Studies on asthma and lung function answered questions mostly on aetiology or risk factors, while natural history and prognosis was more common in studies of rare diseases and other diagnoses. Disease phenotyping was mostly studied in papers on respiratory infectious diseases or rare diseases. Similarly, sample size of the study population also varied by diagnosis of interest (Figure 3b). More than half of the studies on asthma had more than 1000 participants, while 40% of those on rare diseases had less than 100 participants.

The included cohort studies were mostly published in respiratory (103, 28%) or allergy/immunology journals (88, 24%) (Figure 2). Of the individual journals, those with 10 or more papers were either highly specific (Paediatric pulmonology, Paediatric Allergy& Immunology and Journal of Asthma) or high impact respiratory journals (Journal of Allergy and Clinical Immunology, Thorax and European Respiratory Journal). There was only one general journal (PlosONE) with 10 or more included papers (data not shown). There were some differences in the study design, sample size and research question between journals, though the largest differences were observed in the diagnosis of interest (Supplementary Table 2). Papers on asthma were published mainly in allergy/immunology or respiratory journals and those on respiratory infectious diseases in their respective journals. Papers on other diagnoses were more evenly distributed, with the exception of the allergy/immunology journals that published almost exclusively on asthma.

Table 1: Number of manuscripts that accurately followed each of the STROBE checklist items for the reporting of cohort studies from a random subsample (N=100)

	Item No	Recommendation	N
Title and abstract	1	All criteria for item 1	81
		(*a*) Indicate the study's design with a commonly used term in the title or the abstract	83
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	97
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	100
Objectives	3	State specific objectives, including any prespecified hypotheses	97
Methods			
Study design	4	Present key elements of study design early in the paper	93
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	90
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	94
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	84
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	96
Bias	9	Describe any efforts to address potential sources of bias	58
Study size	10	Explain how the study size was arrived at	64
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	92
Statistical methods	12	All criteria for item 12	38
		(*a*) Describe all statistical methods, including those used to control for confounding	92
		(*b*) Describe any methods used to examine subgroups and interactions	83
		(*c*) Explain how missing data were addressed	43
		(*d*) If applicable, explain how loss to follow-up was addressed	59
		(*e*) Describe any sensitivity analyses	66
Results			
Participants	13*	All criteria for item 13 (except c)	72
		(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	78
		(b) Give reasons for non-participation at each stage	76
		(c) Consider use of a flow diagram	-
Descriptive data	14*	All criteria for item 14	56
		(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	90
		(b) Indicate number of participants with missing data for each variable of interest	59
		(c) Summarise follow-up time (eg, average and total amount)	82
Outcome data	15*	Report numbers of outcome events or summary measures over time	98
Main results	16	All criteria item 16 (except c)	82
		(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	84
		(*b*) Report category boundaries when continuous variables were categorized	98

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	85
Discussion			
Key results	18	Summarise key results with reference to study objectives	100
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	94
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	96
Generalisability	21	Discuss the generalisability (external validity) of the study results	51
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	84

Colour code for proportion of manuscripts that reported each item:
<50%; 50-70%; 70-90%; >90%
Items in white were not evaluated as they are not compulsory but should be only 'considered'. We did not evaluate item 6b as none of the studies included were matched.

The reporting quality of the papers was insufficient (Table 1). Only three (0.8%) of the 369 included papers mentioned the STROBE statement in the text, and none of them stated using any other reporting guideline. Of the 100 subsampled publications, only 15% included all the 22 items mentioned in the STROBE checklist. The median number of elements missing from the checklist was 4 (IQR 1-6). The most frequently missed items were a correct description of the efforts to address potential sources of bias (item 9, missing in 42%), the study size explanation (item 10, missing in 36%), description of the statistical methods (item 12, missing in 62%), of the study participants' characteristics (item 14, missing in 44%), and the discussion of the generalisability of the study findings (item 21, missing in 49%). For the reporting of statistical methods and the descriptive data of the study participants (items 12 and 14), one frequent flaw was the lack of description of the number of participants with missing data for each variable (item 14b, missing in 41%) and the explanation of how the missing data were addressed (item 12c, missing in 57%).

Table 2: Association between studies' and journal's characteristics, and the total score on STROBE reporting recommendations for cohort studies' checklist from a Poisson regression (N=100)

	STROBE score		Poisson regression	
	Median	IQR	Crude IRR (95% CI)	Global P value[##]
Society journal: Yes	18	16-21	1.0 (0.9-1.1)	0.562
No	18	15-20		
Journal reporting recommendation				
None	17	16-18	(ref)	0.698
Follow any	19	16-21	1.1 (0.9-1.2)	
Follow STROBE	18	15-21	1.0 (0.9-1.2)	
Attach STROBE checklist	19	14-20	1.0 (0.8-1.2)	
Impact factor			1.0 (1.0-1.1)	0.387
Percentage ranking			1.0 (1.0-1.0)	0.279
Journal category[#]				
Respiratory	18	15-20	(ref)	0.762
Allergy	18	16-20	1.0 (0.9-1.2)	
Paediatrics	18	16-20	1.0 (0.9-1.2)	
General medicine	18	14-20	1.0 (0.8-1.2)	
Infectious diseases	15	15-15	0.9 (0.5-1.4)	
Pub health/epidemiology/environment	19	18-21	1.1 (0.9-1.2)	
Other	22	15-22	1.1 (0.9-1.3)	
Continent of study				
Europe	20	17-21	(ref)	0.493
North America	19	16-21	1.0 (0.9-1.1)	
South America	15	14-16	0.8 (0.6-1.1)	
Africa	16	16-18	0.9 (0.7-1.1)	
Asia	18	13-18	0.9 (0.7-1.03)	
Pacific	16	15-18	0.9 (0.8-1.1)	
Several	21	15-21	1.0 (0.8-1.3)	
Research question				
Aetiology	19	17-21	(ref)	0.078
Natural history / prognosis	18	16-20	1.0 (0.9-1.1)	
Diagnosis	14	14-14	0.7 (0.4-1.3)	
Treatment effects	16	15-17	**0.8 (0.7-0.97)**	
Main diagnosis of interest				
Asthma or wheeze	19	16-21	(ref)	0.825
Respiratory infectious diseases	18	16-18	0.9 (0.8-1.1)	
Rare diseases*	18	15-21	1.0 (0.9-1.1)	
Lung function (healthy children)	20	20-21	1.1 (0.9-1.4)	
Other**	17	16-21	1.0 (0.8-1.2)	

*Rare diseases include: bronchopulmonary dysplasia, diaphragmatic hernia, cystic fibrosis and primary ciliary dyskinesia. **Other diagnoses include: cough, respiratory distress syndrome, pneumothorax and unspecific respiratory symptoms. [#]Categories according to the InCites Journal Citation Report, if a journal appeared in 2 categories, it was classified as the first in which it appears in this order: respiratory, allergy, infectious diseases, public health/epidemiology/environment, paediatrics, general medicine and any other category. [##]**:** Estimated with the likelihood ratio test**.** IQR: inter-quartile range, RCT: randomized controlled trial.

Table 2 shows the results of the univariable Poisson regression analysis of the factors associated with the number of reported items from the STROBE checklist for cohort studies. None of the studied factors was clearly associated with the STROBE score. The journal's characteristics (belonging to a society, impact factor, percentage ranking and journal category), continent of study and main diagnosis of interest were not associated with the STROBE score. Only studies on treatment effects had a lower score (poorer reporting) when compared to those with an aetiological research question (IRR 0.8, 95% CI 0.7-0.97). Table 3 shows the association between these same characteristics and the reporting of 4 specific items (those that had been reported in less than 60% of the manuscripts). As previously, most tested factors were not associated with the reporting of any of the 4 specific items, except for the location of the study, showing a smaller odds to report these items if the study was undertaken in Africa, Asia or the Pacific, compared to Europe. The study of treatment effects or of natural history of disease/prognosis vs. aetiology, had also a lower odds of reporting 3 of the items. As for the journal reporting recommendations, manuscripts published in journals that recommended following any reporting guideline were more likely to discuss the generalisability of the study findings compared to those published in journals with no recommendations.

Table 3: Association between studies' and journal's characteristics, and reporting of the 4 most poorly reported items (<60% of the manuscripts) from a logistic regression (N=100).

	Crude OR (95%CI) for reporting items			
	Item 9 (Bias)	**Item 12 (Statistics)**	**Item 14 (Descriptive)**	**Item 21 (Generalisability)**
Society journal	1.7 (0.7-3.8)	1.7 (0.7-3.9)	1.0 (0.5-2.3)	1.1 (0.5-2.4)
Journal reporting recommendation				
None	(ref)	(ref)	(ref)	(ref)
Follow any guideline	3.0 (0.9-9.5)	1.1 (0.4-3.6)	1.2 (0.4-3.8)	**3.7 (1.1-12.1)**
Follow STROBE	2.0 (0.6-6.1)	1.1 (0.3-3.4)	0.7 (0.2-2.3)	1.2 (0.4-3.8)
Attach STROBE checklist	1.4 (0.3-5.9)	0.9 (0.2-3.9)	0.7 (0.2-3.1)	1.7 (0.4-7.4)
Impact factor	1.1 (0.96-1.2)	1.1 (0.99-1.2)	1.0 (0.9-1.1)	1.1 (0.99-1.2)
Percentage ranking	1.0 (0.9-1.03)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Journal category*				
Respiratory	(ref)	(ref)	(ref)	(ref)
Allergy	2.3 (0.8-6.7)	1.6 (0.5-5.0)	1.8 (0.6-5.1)	0.6 (0.2-1.8)
Paediatrics	0.9 (0.3-3.4)	1.3 (0.3-5.1)	1.5 (0.4-5.3)	0.4 (0.1-1.6)
General medicine	0.5 (0.08-3.5)	2.6 (0.4-15.9)	1.3 (0.2-7.6)	0.3 (0.05-2.2)
Infectious diseases	-	-	-	-
Pub health/epidemiology/ environment	4.9 (0.9-27.3)	1.5 (0.3-6.6)	2.2 (0.5-9.6)	0.8 (0.2-3.3)
Other	1.3 (0.3-5.4)	4.5 (1.0-20.3)	3.4 (0.7-15.9)	1.2 (0.3-5.1)
Continent of study				
Europe	(ref)	(ref)	(ref)	(ref)
North America	0.4 (0.1-1.03)	0.5 (0.2-1.3)	0.7 (0.3-1.9)	1.4 (0.6-3.7)
South America	0.4 (0.2-6.8)	-	-	-
Africa	**0.1 (0.01-0.97)**	0.6 (0.9-4.0)	0.8 (0.1-5.7)	0.6 (0.1-4.0)
Asia	**0.2 (0.05-0.9)**	**0.1 (0.01-0.8)**	0.5 (0.1-1.8)	**0.1 (0.01-0.8)**
Pacific	1.3 (0.2-7.6)	0.5 (0.1-2.1)	**0.2 (0.02-0.9)**	3.1 (0.6-17.2)
Several	0.8 (0.06-9.5)	0.5 (0.04-5.4)	1.1(0.1-13.7)	0.5 (0.04-5.4)
Research question				
Aetiology	(ref)	(ref)	(ref)	(ref)
Natural history / prognosis	1.0 (0.4-2.4)	**0.4 (0.2-0.97)**	0.7 (0.3-1.6)	1.0 (0.4-2.4)
Diagnosis	-	-	-	-
Treatment effects	**0.2 (0.04-0.7)**	-	**0.2 (0.07-0.9)**	0.4 (0.1-1.3)
Main diagnosis of interest				
Asthma or wheeze	(ref)	(ref)	(ref)	(ref)
Respiratory infectious dis.	1.0 (0.3-3.4)	0.6 (0.2-2.0)	1.1 (0.3-3.6)	**0.2 (0.06-0.98)**
Rare diseases*	1.2 (0.4-3.7)	0.5 (0.2-1.6)	0.6 (0.2-1.7)	1.2 (0.4-3.5)
Lung function (healthy)	-	2.5 (0.2-28.7)	1.3 (0.1-15.3)	1.6 (0.1-18.9)
Other**	3.0 (0.6-15.9)	0.2 (0.2-1.3)	0.3 (0.07-1.4)	0.7 (0.2-2.7)

*Rare diseases include: bronchopulmonary dysplasia, diaphragmatic hernia, cystic fibrosis and primary ciliary dyskinesia. **Other diagnoses include: cough, respiratory distress syndrome, pneumothorax and unspecific respiratory symptoms. #Categories according to the InCites Journal Citation Report, if a journal appeared in 2 categories, it was classified as the first in which it appears in this order: respiratory, allergy, infectious diseases, public health/epidemiology/environment, paediatrics, general medicine and any other category. IQR: inter-quartile range, RCT: randomized controlled trial.

Discussion

Summary of main findings

This systematic review found that reporting quality of cohort studies on paediatric lower respiratory problems was insufficient; only 15% of the manuscripts included all the recommended items from the STROBE checklist and 42-63% missed specific items such as a correct description of statistical methods**.** Most published paediatric cohort studies were based in Europe and North America, answering research questions on aetiology and risk factors, and centred on asthma or wheeze. The most frequently used design were birth cohorts with only limited use of alternative strategies that may reduce the costs of cohort studies, such as record linkage or nested case-control studies. Finally, most studies were published in specialised respiratory or allergy journals.

Interpretation of results

During the screening process, we found that one fifth (101) of the 521 excluded full-text papers were actually not cohort studies (77) or did not use a longitudinal analysis (24), despite appearing in a search using specific search terms such as “cohort” or “follow-up”, and although we had already excluded papers based on the information in the title or abstract. This was sometimes due to the incorrect use of the word “cohort” and the absence of a clear description of the study design in the abstract or title. This information was still missing in 17% of the included manuscripts. The cohort studies on paediatric lower respiratory problems in 2018 that we analysed, focused mostly on aetiology of asthma and were based in Europe or North America. Lower respiratory infectious diseases, such as pneumonia or tuberculosis, which are a major cause of death in children under 5 years of age worldwide [9], were the focus of only 15% of the studies. This may be because most of the studies are based in high income countries, whereas the burden of respiratory infectious diseases is much higher in low and middle-income countries [9]. The most commonly used design was the birth or pregnancy cohort study. This is

an excellent design to study early life factors and their influence on disease, but also quite expensive as it needs a large sample size to achieve an adequate number of children with a specific outcome and a long follow-up. Adaptations of cohort studies that are cheaper such as case-control studies nested in cohort studies were rarely used (3%). Linking available routine data is often an elegant way to obtain a cohort dataset with little or no selection bias or attrition bias, and achieve large sample sizes at a low cost (even whole population studies)[10]. As a disadvantage, studies based on linked routine data often lack clinically relevant details on exposure and outcome, resulting in measurement bias. This design was used in one quarter (85) of the included studies, and limited to countries with adequate electronic record keeping and unique personal identifiers (such as the social security number) that enables linkage between different datasets.

Even though reporting quality of observational studies improved after the publication of the STROBE statement [6], current studies in different medical fields have shown that adherence to STROBE reporting criteria remains poor or at most moderate [2-7,11-15]. Poor reporting quality does not necessarily imply that the conduct and analysis of the study has been poor. On the other hand, a high STROBE score does not allow to conclude that the study planning and conduct have been excellent. But good reporting is essential, as it enables readers and reviewers to assess the quality and risk of bias of a study. For example, we cannot assess attrition bias if authors do not report how many participants were lost to follow-up in a cohort study. There are multiple tools available to assess the methodological quality or the risk of bias of observational studies [16], such as the Newcastle-Ottawa Scale, an easy tool that assesses the quality of non-randomised studies included in a systematic review based on the selection of the study groups, the comparability of the groups, and the ascertainment of the exposure or outcome of interest [17]. The items we identified as being frequently missed, such as the description of statistical methods, the sample size estimation or the potential sources of bias have been also reported in previous studies [3,6,7,11,12,14,15]. These items are essential to

enable other researchers to reproduce the study and to evaluate its internal and external validity. The handling of missing information was insufficiently reported in the papers included in this review, both in the methods (43% of papers) and results (59%) section, resulting in a possible source of bias. Missing data and loss to follow up are common limitations of cohort studies, but the implementation of specific statistical strategies, like multiple imputation or inverse probability weighting [18], may attenuate its impact. Reporting bias and confounding is even more important in cohort studies analysing causal associations. Experts recommend specific strategies for adequate variable selection and interpretation of results in causal inference studies, such as the use of Direct Acyclic Graphs to identify possible confounders and mediators [19], and the presentation of effect estimates with their measures of variability (confidence intervals) instead of P values in isolation [20]. These strategies were discussed in a recent editorial by editors of respiratory, sleep, and critical care journals, where they also highlighted the importance of adhering to STROBE guidelines when reporting sources of bias and confounding [21].

A plausible reason for not reporting all the STROBE items may be the limitation of manuscript's length, reducing the amount of information that may be included in the paper. Although most journals offer the possibility of including supplementary online text and tables, they should adjust their policies and guidelines to ensure authors are able to comply with reporting guidelines. For example, to allow longer titles to include the study design, and longer methods sections to encourage a more detailed description of the statistical methods (e.g. handling of missing data and identification of confounders). On the other hand, authors may not be aware of the existence of the STROBE statement [22] or they may deliberately omit certain information such as missing data to increase the publication chances. In this case, it is the journals' responsibility to inform the authors about the different reporting guidelines for each study design. Cohort studies may need to also adhere to other reporting guidelines depending on the aim of the manuscript, such as the TRIPOD (Transparent reporting of a multivariable

prediction model for individual prognosis or diagnosis)[23], or to specific STROBE extensions, such as RECORD (REporting of studies Conducted using Observational Routinely-collected health Data)[24]. There are several other STROBE extensions for specific clinical areas, but these all include additional criteria to the basic STROBE checklist, so the standard criteria remain valid. We did not assess the adherence to any other reporting guideline, but none of the 100 subsampled manuscripts stated using them. These reporting guidelines are all listed in the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network homepage [25]. Journals should promote adherence to reporting guidelines through a compulsory attachment of the reporting checklist at submission and as an online supplement for readers. In addition, journals should implement further measures such as involving reviewers in checking reporting quality or even employing a journal methodologist to check manuscripts substantially before final acceptance. Only by applying this measure in a strict way, as it is done with randomized controlled trials, will the reporting quality of observational studies improve and become standardised.

Quality of reporting was not associated with the characteristics of the journal in our study. It did not depend on the journal's impact factor, percentage ranking, society ownership, category (by subject), or reporting recommendations. Similarly, it was not associated with the study's location, research question or main diagnosis of interest, except for a decreased STROBE score of papers reporting on treatment effects compared to aetiology. Previous studies have found quality of reporting of observational studies to be associated with some of these factors, such as the journal's impact factor [7] and authors guidelines [6], the publication type (peer-reviewed vs report) [3,5] or the author's affiliation (public health agency vs academic) [5]. However, these findings are not consistent [15] and are sometimes based on small samples (<80 manuscripts) in specific fields. This shows that reporting quality of cohort studies in paediatric respiratory research needs to be improved globally.

Strengths and limitations

This systematic review is the first to describe the characteristics of cohort studies reporting on paediatric lower respiratory problems published recently and to assess their reporting quality according to the STROBE statement. We collected detailed information on a large number of studies published worldwide. However, the review has some limitations. First, we did not extend our search to specific databases from South America, Africa or Asia and limited the included studies to those published in English. This may have been one of the reasons for the under-representation of these regions of the world. However, the most important and relevant studies are normally published in English and indexed in Medline or Embase to increase accessibility. Second, the large number of studies included precluded a duplicate screening and data extraction. This may be more relevant for the evaluation of the STROBE checklist items, some of which may be rather subjective. However, all assessors were from the same research team; we used well-defined criteria for manuscript inclusion and exclusion, and for the assessment of adherence to each of the STROBE checklist's elements; and papers where the assessor was uncertain, were discussed in the team until agreement was reached.. Third, the criteria we used to evaluate the adherence to each of the STROBE checklist's items were not very strict. For example, when evaluating the information on confounders or reporting of limitations, we only evaluated if confounders were considered or if limitations were mentioned. We did not study in detail each manuscript to assess if the confounders included or the limitations described were correct and complete. Therefore, our evaluation of the reporting quality is quite optimistic and reporting quality may be even poorer.

Conclusion

The findings of this review may inform both authors and editors on how to increase reporting quality of papers of cohort studies reporting on paediatric lower respiratory problems and what areas of research are neglected. Researchers should follow reporting guidelines (either STROBE

or as appropriate) closely when submitting a manuscript and should check these when reviewing other researchers' manuscripts. The use of nested case-control studies, well designed retrospective chart reviews and linkage of routine data with study data should be borne in mind when designing a cohort study to reduce costs. On the other side, editors from international journals should encourage the publication of studies focused on lower respiratory infections and rare diseases, and those based in low and middle-income countries. Journals should not only endorse the STROBE statement for the reporting of cohort studies, but should demand authors to attach the STROBE checklist during the submission process and ask reviewers to report any missing item in the manuscript. Only through a joined effort of editors, reviewers and authors may we improve the reporting quality of paediatric cohort studies on respiratory problems.

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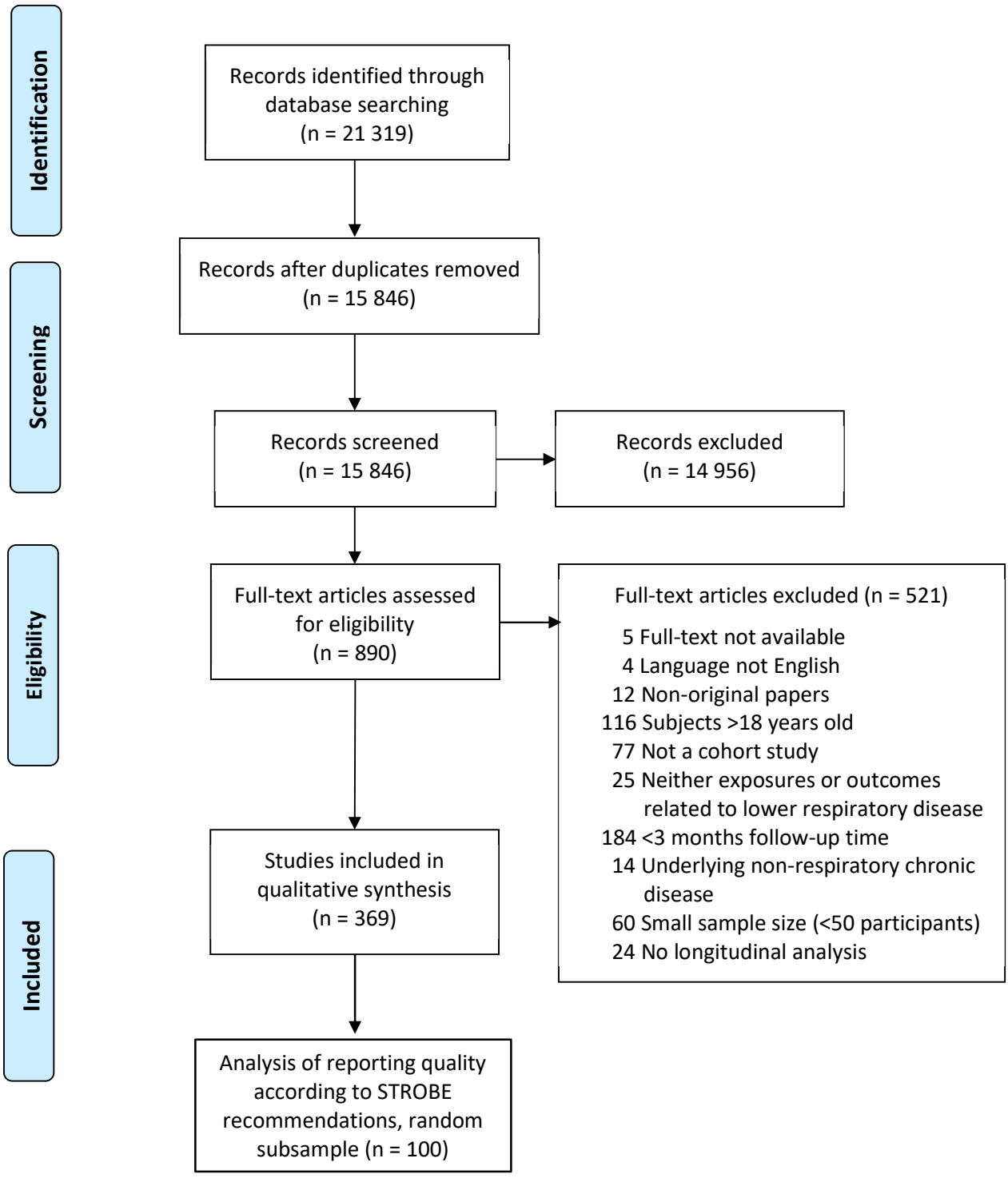
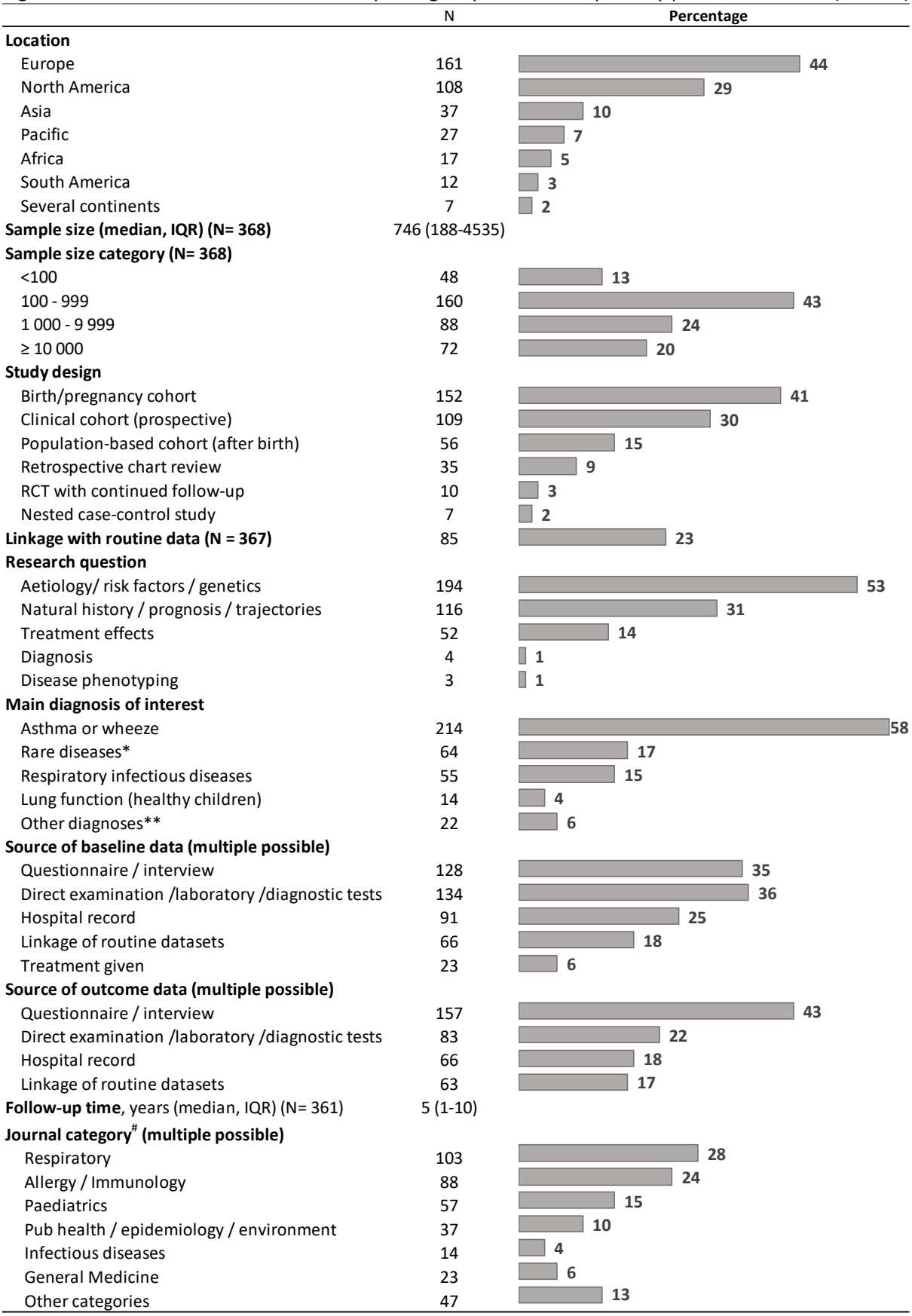


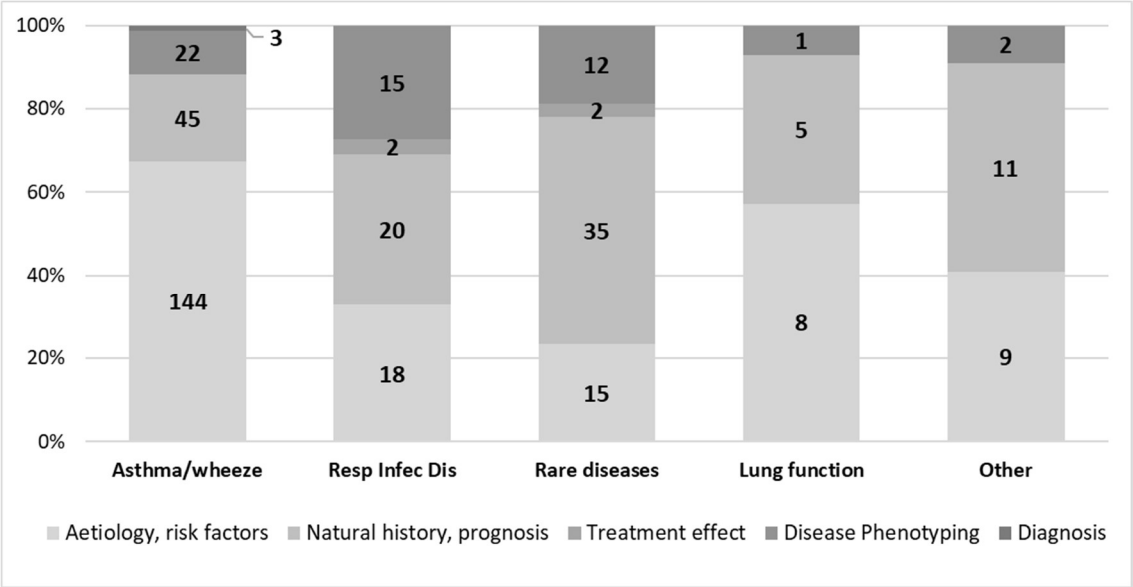
Figure 1: Flow diagram of included and excluded studies.

Fig. 2: Characteristics of cohort studies reporting on paediatric respiratory problems in 2018 (N= 369)



*Rare diseases include: bronchopulmonary dysplasia, diaphragmatic hernia, cystic fibrosis and primary ciliary dyskinesia.
**Other diagnoses include: cough, respiratory distress syndrome, pneumothorax and unspecific respiratory symptoms.
#Categories according to the InCites Journal Citation Report, if a journal appeared in 2 categories, it was classified as the first in which it appears in this order: respiratory, allergy, infectious diseases, public health/epidemiology/environment, paediatrics, general medicine and any other category. IQR: inter-quartile range, RCT: randomized controlled trial.

A. Research question by diagnosis of interest



B. Sample size by diagnosis of interest

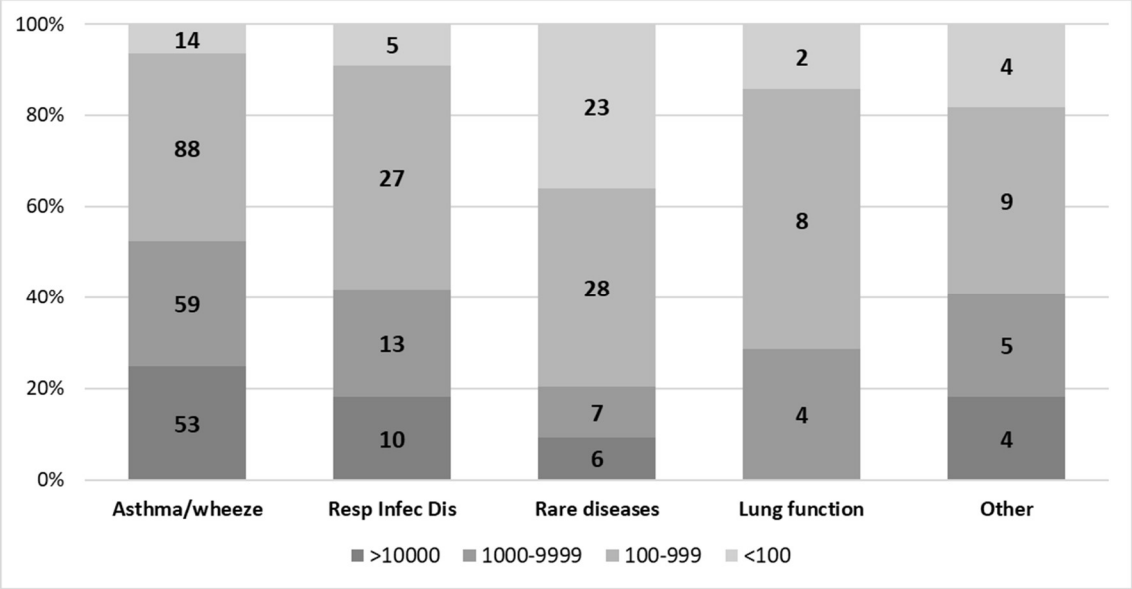


Figure 3: Type of research question (A) and sample size (B) by diagnosis of interest, of cohort studies reporting on paediatric respiratory outcomes or exposures in 2018 (N= 369).

The number inside each bar is the total number of manuscripts for each section.

Supplementary Text

Search terms used for Medline (Ovid)

1. exp cohort studies /

2. (cohort* or prospectiv* or longitudinal* or nested or retrospectiv* or follow*).ti,ab,kw.

3. exp pediatrics/ or exp adolescent/ or exp child/ or exp infant/

4. (toddler* or infan* or child* or schoolchild* or adolescen* or teen* or pediatr* or paediatr*).ti,ab,kw

5. exp "Respiratory Tract Diseases"/ or exp "signs and symptoms, respiratory"/

6. (asthma* or wheez* or bronch* or trache* or laryng* or "vocal cord*" or "primary ciliary dyskinesia" or "cystic fibrosis" or "lung disease*" or "lung infection" or respirat* or cough* or dyspn* or pneumo* or pleura* or pulmonar* or chest or thora* or empyema or "lung abscess" or legionell* or tuberculos* or aspergill* or blastomycos* or "syncytial virus").ti,ab,kw.

7. exp Respiratory Function Tests/

8. ("Airway Resistance" or "Blood Gas Analysis" or Oximetry or Capnography or "Exercise Test*" or "Lung Compliance" or "Lung Volume" or "Lung Capacity" or Plethysmography or "Ventilation-Perfusion" or "forced expiration" or "expiratory flow" or "expiratory volume" or "Maximal Voluntary Ventilation" or "maximal expiratory" or spirometry or "Valsalva Maneuver" or "lung function" or "lung examination" or sputum or "lung biopsy" or "multiple breath washout" or "transthoracic" or "lung angiography" or "lung lavage").ti,ab,kw.

9. exp respiration/

10. (breathing or "breath holding" or exhalation or inhalation or "mucociliary clearance" or "lung clearance" or "lung diffusion" or "lung gas exchange" or "lung mechanics" or "lung ventilation").ti,ab,kw.

11. 1 or 2

12. 3 or 4

13. 5 or 6 or 7 or 8 or 9 or 10

14. 11 and 12 and 13

15. limit 14 to english language

16. limit 15 to year='2018'

TOTAL: 7610 references

Supplementary Table 1: Classification of journals according to the categories used by the In Cites Journal Citation Report.

Respiratory	- American Journal of Respiratory & Critical Care Medicine - Annals of the American Thoracic Society - BMC Pulmonary Medicine - ERJ Open Research - European Respiratory Journal - International Journal of Tuberculosis & Lung Disease - Journal of Asthma - Journal of asthma and allergy - Journal of Cystic Fibrosis - Journal of Thoracic Disease - NPJ Primary Care Respiratory Medicine - Pediatric Pulmonology - Respiratory Care - Respiratory Medicine - Respiratory Physiology & Neurobiology - Respiratory Research - The Lancet Respiratory Medicine - Thorax
Allergy/immunology	- Allergologia et Immunopathologia - Allergology International - Allergy - Allergy & Asthma Proceedings - Allergy: European Journal of Allergy and Clinical Immunology - Annals of Allergy, Asthma, & Immunology - Asian Pacific Journal of Allergy & Immunology - Asim, Allerji, Immunoloji - Clinical & Experimental Allergy - Journal of Allergy & Clinical Immunology - Journal of Allergy & Clinical Immunology: In practice - Journal of Immunology - Journal of Investigational Allergology & Clinical Immunology - Pediatric Allergy & Immunology - World Allergy Organization Journal
Epidemiology, public health and environmental	- American Journal of Epidemiology - BMC Public Health - Clinical Epidemiology - Epidemiology - Epidemiology & Infection - European Journal of Epidemiology - International Journal of Epidemiology - Iranian Journal of Allergy Asthma & Immunology - Journal of Epidemiology & Community Health - Public Health - Archives of Environmental & Occupational Health - Atmospheric Environment - Environment International - Environmental Epidemiology - Environmental Health Perspectives - Environmental Health: A Global Access Science Source - Environmental Research - Environmental Science & Pollution Research - International Journal of Environmental Research & Public Health - Science of the Total Environment

Paediatrics	- Acta Paediatrica - American Journal of Perinatology - Archives of Disease in Childhood - BMC Pediatrics - BMJ Paediatrics Open - Clinical Pediatrics - Early Human Development - Egyptian Pediatric Association Gazette - European Journal of Pediatrics - International Journal of Pediatrics - Jornal de Pediatria - Journal of Adolescent Health - Journal of Pediatrics - Journal of Perinatology - Maternal & Child Health Journal - Minerva Pediatrica - Neonatology - Paediatrics & Child Health - Pediatric Research - Pediatrics - Pediatrics & Neonatology - Prenatal Diagnosis - Revista Paulista de Pediatria - The Lancet Child & Adolescent Health
Infectious diseases	- AIDS Research & Human Retroviruses - Antibiotics - Clinical Infectious Diseases - Emerging Infectious Diseases - European Journal of Clinical Microbiology & Infectious Diseases - Journal of Infectious Diseases - Journal of Medical Virology - Journal of Microbiology, Immunology & Infection - Open Forum Infectious Diseases - Pediatric Infectious Disease Journal - Vaccine
General Medicine	- African Health Sciences - BioMed Research International - Bjgp Open - BMJ Open - Bosnian Journal of Basic Medical Sciences - Colombia Medica - Cureus - Eastern Mediterranean Health Journal - eLife - Eurosurveillance - International journal of general medicine - JAMA Pediatrics - Jci Insight - Nature Communications - PeerJ - PLoS ONE - Revista Da Associacao Medica Brasileira - Sao Paulo Medical Journal = Revista Paulista de Medicina - Saudi Medical Journal - Scientific Reports - Southern Medical Journal

Other	- Acta Obstetricia et Gynecologica Scandinavica - American Journal of Clinical Nutrition - American Journal of Managed Care - American Journal of Obstetrics & Gynecology - American Journal of Respiratory Cell & Molecular Biology - American Journal of Tropical Medicine & Hygiene - Annals of Behavioral Medicine - Annals of Surgery - Arthritis care & research - British Journal of Dermatology - British Journal of Nutrition - CJEM Canadian Journal of Emergency Medical Care - Clinical Nutrition - Clinical Otolaryngology - ClinicoEconomics and Outcomes Research - CMAJ - European Journal of Clinical Nutrition - European Journal of Obstetrics, Gynecology, & Reproductive Biology - European Journal of Psychotraumatology - European Radiology - Frontiers in Pharmacology - Frontiers in Physiology - Health Promotion Practice - Health Services Insights - Hypertension - International Journal of Eating Disorders - Journal of Laparoendoscopic & Advanced Surgical Techniques. - Journal of Pediatric Gastroenterology & Nutrition - Journal of Pediatric Nursing - Journal of Pediatric Surgery - Journal of Racial & Ethnic Health Disparities - Journal of Voice - Maternal & Child Nutrition - Metabolomics - Nature Plants - Nutrients - Oncotarget - Orphanet Journal Of Rare Diseases - Pediatric Critical Care Medicine - Pharmacoepidemiology & Drug Safety - Postepy Dermatologii I Alergologii - Psychology & Health - Ultrasound in obstetrics & gynecology

Supplementary Table 2: Characteristics of cohort studies reporting on paediatric respiratory outcomes or exposures in 2018, by journal categories (N=369)[#]

	Respira-tory (N=103)	Allergy/ Immun (N=88)	Resp. infect dis. (N=14)	PH /epi /envir. (N=37)	Paedia-trics (N=57)	General med. (N=23)	Other (N= 47)
Location							
Europe	45 (44)	40 (45)	3 (21)	17 (46)	23 (40)	6 (26)	27 (57)
North America	31 (30)	21 (24)	6 (43)	9 (24)	23 (40)	6 (26)	12 (26)
South America	2 (2)	3 (3)	0	0	3 (5)	4 (17)	0
Africa	4 (4)	5 (6)	0	3 (8)	1 (2)	3 (13)	1 (2)
Asia	6 (6)	14 (16)	2 (14)	4 (11)	3 (5)	4 (17)	4 (9)
Pacific	10 (10)	4 (5)	3 (21)	3 (8)	4 (7)	0	3 (6)
Several continents	5 (5)	1 (1)	0	1 (3)	0	0	0
Sample size (median, IQR) (N= 368)	564 (144-3277)	769 (250-2892)	1403 (158-15504)	3537 (641-23100)	701 (145-4475)	432 (77-10476)	664 (161-9038)
Sample size category (N= 368)							
<100	20 (19)	5(6)	1 (7)	1 (3)	8 (14)	6 (26)	7(15)
100 - 999	42 (41)	46 (52)	5 (36)	11 (30)	26 (46)	8 (35)	22(47)
1 000 – 9 999	28 (27)	25 (28)	4 (29)	11 (30)	10 (18)	3 (13)	7(15)
≥ 10 000	13 (13)	12 (14)	4 (29)	14 (38)	13 (23)	6 (26)	11(23)
Study design							
Birth/pregnancy cohort	44 (43)	42 (48)	2 (14)	20 (54)	22 (39)	5 (22)	17(36)
Population-based (after birth)	12 (12)	10 (11)	2 (14)	10 (27)	8 (14)	6 (26)	8(17)
Clinical cohort (prospective)	31 (30)	28 (32)	9 (64)	6 (16)	14 (25)	7 (30)	14(30)
Retrospective chart review	13 (13)	0	0	0	12 (21)	4 (17)	6(13)
Nested case-control	1 (1)	3(3)	1(7)	0	0	1 (4)	1(2)
RCT with continued follow-up	2 (2)	5 (6)	0	1(3)	1 (2)	0	1(2)
Linkage with routine data (N= 367)	18(18)	19 (22)	5 (36)	10 (27)	13 (23)	5 (22)	15(32)
Research question							
Aetiology	42(41)	50 (57)	4 (29)	27 (73)	27 (47)	15 (65)	29(62)
Natural history / prognosis	40(39)	28 (32)	7 (50)	4 (11)	20 (35)	4 (17)	13(28)
Diagnosis	4 (4)	0	0	0	0	0	0
Treatment effects	17(17)	8 (9)	3 (21)	5 (14)	10 (18)	4 (17)	5 (11)
Aetiology	0	2 (2)	0	1 (3)	0	0	0
Main diagnosis of interest							
Asthma or wheeze	56 (54)	72 (82)	1(7)	25 (68)	22 (39)	13 (57)	25(53)
Respiratory infectious dis.	7 (7)	11 (13)	9 (64)	5 (14)	14 (25)	4 (17)	5 (11)
Rare diseases*	27(26)	0	4 (29)	0	16 (28)	4 (17)	13(28)
Lung function (healthy)	7 (7)	1 (1)	0	4 (11)	0	0	2 (4)
Other**	6 (6)	4 (5)	0	3 (8)	5 (9)	2 (9)	2 (4)

Figures represent 'n (%)' unless otherwise stated *Rare diseases include: bronchopulmonary dysplasia, diaphragmatic hernia, cystic fibrosis and primary ciliary dyskinesia. **Other diagnoses include: cough, respiratory distress syndrome, pneumothorax and unspecific respiratory symptoms. IQR: inter-quartile range, RCT: randomized controlled trial, CF: cystic fibrosis, PCD: Primary ciliary dyskinesia.